We claim:

1. A method for the identification of at least one member of a pair or complex of interacting molecules from a pool of potentially interacting molecules, comprising:

(A) providing at least one set of host cells, each set containing at least one genetic element comprising a selectable marker, said selectable marker being different between different sets of host cells, said genetic elements each comprising genetic information specifying one of said potentially interacting molecules, said host cells further carrying a readout system that is activated upon the presence of auto-activating molecules;

(B) selecting against host cells expressing a molecule able to auto-activate the readout system by transferring at least one set of host cells or progeny of at least one set of host cells to at least one selective medium which allows growth of said host cells in the presence of said selectable marker different for each set of host cells and which precludes growth of said host cells upon auto-activation of said readout system;

(C) combining in host cells at least two genetic elements, wherein at least one set of host cells grows on said selective medium specified in (B);

(D) allowing at least one interaction, if any, to occur;

(E) selecting for said interaction by transferring said host cells or progeny of said host cells to a selective medium that allows identification of said host cells upon activation of the readout system;

(F) identifying host cells that contain interacting molecules that activate said readout system on said selective medium;

(G) identifying at least one member of said pair or complex of interacting molecules;

wherein said host cells are not yeast cells.

2. A method for the identification of at least one member of a pair or complex of interacting molecules from a pool of potentially interacting molecules, comprising:

(A) providing at least one set of host cells, each set containing at least one genetic element comprising a selectable marker, said selectable marker being different between different sets of host cells, said genetic elements each comprising genetic information

specifying one of said potentially interacting molecules, said host cells further carrying a readout system that is activated upon the presence of auto-activating molecules;

(B) selecting against host cells expressing a molecule able to auto-activate the readout system by transferring at least one set of host cells or progeny of at least one set of host cells to at least one selective medium which allows growth of said host cells in the presence of said selectable marker different for each set of host cells and visual differentiation between those cells whose readout system has been activated from those host cells whose readout system has not been activated;

(C) combining in host cells at least two different genetic elements, wherein at least one set of host cells grows on said selective medium specified in (B);

(D) allowing at least one interaction, if any, to occur;

(E) selecting for said interaction by transferring said host cells or progeny of said host cells to a selective medium that allows identification of said host cells upon activation of the readout system;

(F) identifying host cells that contain interacting molecules that activate said readout system on said selective medium;

(G) identifying at least one member of said pair or complex of interacting molecules

3. A method for the identification of at least one member of a pair or complex of interacting molecules from a pool of potentially interacting molecules, comprising:

(A) providing at least one set of host cells, each set containing at least one genetic element comprising a selectable marker, said selectable marker being different between different sets of host cell, said genetic elements each comprising genetic information specifying one of said potentially interacting molecules, said host cells further carrying a readout system that is activated upon the presence of auto-activating molecules;

(B) selecting against host cells expressing a molecule able to auto-activate the readout system by transferring at least one set of host cells or progeny of at least one set of host cells to at least one selective medium which allows growth of said host cells in the presence of said selectable marker different for each set of host cells and which precludes growth of said host cells upon auto-activation of said readout system;

(C) combining in host cells at least two genetic elements, wherein at least one set of host cells grows on said selective medium specified in (B);

(D) allowing at least one interaction, if any, to occur;

(E) selecting for said interaction by transferring said host cells or progeny of said host cells to a selective medium that allows identification of said host cells upon activation of the readout system;

(F) identifying host cells that contain interacting molecules that activate said readout system on said selective medium;

(G) identifying at least one member of said pair or complex of interacting molecules;

wherein said host cells are yeast cells, and at least one of the steps (B), (C), (E) or (F) is effected or assisted by automation using regular grid patterns of host cells.

4. The method of claim 1, wherein said pair or complex of interacting molecules is selected from the group consisting of RNA-RNA, RNA-DNA, RNA-protein, DNA-DNA, DNA-protein, protein-peptide, peptide-peptide or protein-protein interactions.

5. The method of claim 1, wherein said genetic elements are plasmids, artificial chromosomes, viruses or other extrachromosomal elements.

6. The method of claim 1, wherein said interaction leads to the formation of a transcriptional activator comprising a DNA-binding and a transactivating protein domain and which is capable of activating a response moiety driving the activation of said readout system.

7. The method of claim 1, wherein said readout system comprises at least one counterselectable gene.

8. The method of claim 7, wherein said counterselectable gene is one of the genes URA3, LYS2, sacB, CAN1, CYH2, rpsL, or lacY.

9. The method of claim 7, wherein the selective medium in step (B) comprises a counterselective compound.

10. The method of claim 9, wherein said counterselective compound is 5-fluoro orotic acid, canavanine, cycloheximide, sucrose, tONPG or streptomycin.

11. The method of claim 2, wherein said readout system comprises or further comprises at least one detectable protein.

12. The method of claim 11, wherein said detectable protein is encoded from at least one of the genes lacZ, HIS3, URA3, LYS2, tetA, sacB, gfp, yfp, bfp, cat, luxAB, HPRT bla, kan or a surface marker.

13. The method of claim 1, wherein said host cells are bacterial cells, mammalian cells, insect cells or plant cells.

14. The method of claim 1, further comprising transforming, infecting or transfecting at least one set of host cells of said sets of host cells with said genetic element or genetic elements prior to step (D).

15. The method of claim 1, further comprising transforming, infecting or transfecting each set of host cells of said sets of host cells with said genetic elements prior to step (D).

16. The method of claim 1, further comprising transforming, infecting or transfecting one set of host cells of said sets of host cells with at least one genetic element prior to step (A), selecting against host cells in said one set of host cells expressing a molecule able to auto-activate said readout system as specified in step (B), and transforming, infecting or transfecting said set of host cells with at least one further genetic element in step (D).

17. The method of claim 1, wherein cell fusion, conjugation or interaction mating is used for the generation of said host cells with said genetic elements prior to step (D), preferably in step (C).

18. The method of claim 17, wherein said cell fusion, conjugation or interaction mating is affected or assisted by automation.

19. The method of claim 18, wherein said automation is effected by an automated picking, spotting, rearraying pipetting, micropipetting or cell sorting device.

20. The method of claim 19, wherein said device is a picking robot, spotting robot, rearraying robot, pipetting system, micropipetting system or fluorescent assisted cell sorting (FACS) system.

21. The method of claim 1, wherein said selectable marker is an auxotrophic or antibiotic marker.

22. The method of claim 21, wherein said auxotrophic or antibiotic marker is LEU2, TRP1, URA3, ADE2, HIS3, LYS2, kan, bla, Zeocin, neomycin, hygromycin, pyromycin or G418.

23. The method of claim 1, wherein host cells or progeny of host cells of step (D) are transferred to a storage compartment.

24. The method of claim 23, wherein the transfer to a storage compartment is effected or assisted by automation.

25. The method of claim 23, wherein the transfer to a storage compartment is effected by an automated arraying, replicating, picking, spotting, pipetting or micropipetting or cell sorting device.

26. The method of claim 25, wherein said device is a picking robot, spotting robot, pipetting system, micropipetting system or fluorescent assisted cell sorting (FACS) system.

27. The method of claim 23, wherein said storage compartment comprises an anti-freeze agent.

28. The method of claim 23, wherein said storage compartment is at least one microtitre plate.

29. The method of claim 28, wherein said at least one microtitre plate comprises 96, 384, 846 or 1536 wells.

30. The method of claim 1, wherein the transfer of host cells or progeny of host cells in step (E) is effected or assisted by automation using a regular grid pattern.

31. The method of claim 30, wherein the transfer of host cells or progeny of host cells in step (E) is effected by an automated replicating, picking, spotting, pipetting or micropipetting or cell sorting device.

32. The method of claim 31, wherein said device is a replicating robot, picking robot, spotting robot, pipetting system, micropipetting system or fluorescent assisted cell sorting (FACS) system.

33. The method of claim 30, wherein the transfer of host cells or progeny of host cells in step (E) is made by multiple transfers carrying additional host cells to the same position in said regular grid pattern.

34. The method of claim 1, wherein the transfer of host cells or progeny of host cells in step (E) is made to at least one carrier.

35. The method of claim 34, wherein said at least one carrier is a microtitre plate and the regular grid pattern is at densities greater than 1, preferably greater than 4, more preferably greater than 10, most preferably greater than 18 clones per centimeter square.

36. The method of claim 34, wherein said at least one carrier is a porous support and the regular grid pattern is at densities in the range of 1 to 10, preferably 10 to 50, more preferably 50 to 100, most preferably greater than 100 clones per centimeter square.

37. The method of claim 34, wherein said at least one carrier is a non-porous support and the regular grid pattern is at densities in the range of 1 to 100, preferably 100 to 500, more preferably 500 to 1000, most preferably greater than 1000 clones per centimeter square.

38. The method of claim 1, wherein the identification of host cells in step (F) from consideration of the activation state of said readout system using visual means is effected or assisted by automation.

39. The method of claim 1, wherein the identification of host cells in step (F) from consideration of the activation state of said readout system is effected or assisted by automated digital image capture, storage, processing, and/or analysis.

40. The method of claim 1, wherein the identification of said at least one member of said pair or complex of interacting molecules in step (G) is effected by nucleic acid hybridisation, oligonucleotide hybridisation, nucleic acid or protein sequencing, restriction digestion, spectrometry or antibody reactions.

41. The method of claim 1, wherein the identification of said at least one member of said pair or complex of interacting molecules in step (G) is effected using a regular grid pattern of said at least one member or of said genetic information encoding said at least one member.

42. The method of claim 41, wherein construction of regular grid patterns in step (G) is effected or assisted by automation.

43. The method of claim 42, wherein the automation is effected or assisted by an automated spotting, pipetting or micropipetting or cell sorting device.

44. The method of claim 43, wherein automation in step (G) is implemented by employing a spotting robot, spotting tool, pipetting system or micropipetting system.

45. The method of claim 41, wherein said identification is effected by automated digital image capture, storage, processing and/or analysis.

46. The method of claim 1, wherein nucleic acid molecules, prior to said identification in step (G), are amplified by PCR or are amplified in a different host cell as a part of said genetic elements, preferably in bacteria and most preferably in E. coli.

47. The method of claim 1, further comprising:

(H) providing at least one of said genetic elements in step (A), which additionally comprises or comprise a counterselectable marker, wherein said counterselectable markers are different for each type of genetic element;

(I) selecting for interaction by transferring host cells or progeny of host cells in step (E) to

(i) at least one selective medium that precludes growth of host cells in the presence of the counterselectable marker specified in (H) and allows growth in the presence of a selectable marker; and

(ii) a further selective medium that allows identification of host cells upon activation of the readout system;

(J) identifying host cells in step (F) that contain interacting molecules that:

(iii) do not activate said readout system on said at least one selective medium specified in (i); and

(iv) activate said readout system on said selective medium specified in (ii).

1. The method of claim 47, wherein the genetic element that additionally comprises a counterselectable marker further specifies an activation domain fusion protein.

2. The method of claim 1, further comprising:

(K) providing at least two of said genetic elements in step (A), which additionally comprise different counterselectable markers;

(L) selecting for interaction by transferring host cells or progeny of host cells in step (E) to

(v) at least one selective medium, wherein said selective medium that precludes growth of host cells in the presence of the first counterselectable marker of the counterselectable markers specified in (K) and allows growth in the presence of a first selectable marker;

(vi) at least one selective medium, wherein said selective medium precludes growth of host cells in the presence of the second counterselectable marker of the counterselectable markers specified in (K) and allows growth in the presence of a second selectable marker;

(vii) a further selective medium that allows identification of said host cells upon activation of the readout system; and

(M) identifying host cells that contain molecules that:

(viii) do not activate said readout system on said at least one selective medium specified in (v); and

(ix) do not activate said readout system on said at least one selective medium specified in (vi); and

(x) activate said readout system on said selective medium specified in (vii).

3. The method of claim 49, wherein said at least two genetic elements that additionally comprise a counterselectable marker further specify a DNA binding domain fusion protein and an activation domain fusion protein, respectively.

4. The method of claim 47, wherein said counterselectable marker or counterselectable markers of step (H) or (K) are selected from the group of URA3, LYS2, sacB, CAN1, CYH2, rpsL or lacY.

5. The method of claim 47, wherein the transfer of host cells or progeny of host cells in step (I) or (L) is effected or assisted by automation.

6. The method of claim 52, wherein the said automation in step (I) or (L) is effected by an automated replicating, picking, spotting, pipetting or micropipetting or cell sorting device.

7. The method of claim 53, wherein said automation in step (I) or (L) is implemented by employing a replicating robot, picking robot, spotting robot, spotting tool, automated pipetting or micropipetting system, or fluorescent assisted cell sorting (FACS) system.

8. The method of claim 2, wherein said visual differentiation in step (B) is based on a difference between host cells in different activation states of the readout system which can be detected by visual means.

9. The method of claim 55, wherein said difference between host cells in different activation states that can be detected by visual means is brought about by activation of one of the genes lacZ, gfp, yfp, bfp, CAT, luxAB, or of a surface marker.

57. The method of claim 55, wherein said visual means include digital image capture, storage, processing and/or analysis.

58. The method of claim 1, wherein said genetic information specifying one of said potentially interacting molecules is different for each host cell in a set of host cells or a majority of host cells in a set of host cells.

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59. The method of claim 58, wherein said genetic information specifying one of said potentially interacting molecules is identical in not more than 10 %, preferably not more than 5 %, more preferably not more than 2 %, most preferably not more than 1 % of host cells in a set of host cells.

60. A method for the production of a pharmaceutical composition comprising formulating at least one member of the interacting molecules identified by the methods of claim 1 in a pharmaceutically acceptable form.

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61. A method for the production of a pharmaceutical composition comprising formulating an inhibitor of the interaction of the interacting molecules identified by the methods of claim 1 in a pharmaceutically acceptable form.

62. A method for the production of a pharmaceutical composition comprising identifying a further molecule of a cascade of interacting molecules of which at least one of said interacting molecules identified by the methods of claim 1 is a part of or identifying an inhibitor of the function of said further molecule.

63. Kit comprising:

(N) Host cells, comprising a readout system which allows host cells to be counterselected against auto-activation of said readout system; and

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(O) at least one genetic element comprising a selectable marker, a counterselectable marker and genetic information encoding an activation domain or a DNA binding domain, which activation domain and DNA binding domain are together able to activate said readout system;

wherein said host cells are not yeast cells.

64. Kit according to claim 63, wherein said host cells are bacterial cells.

65. Kit comprising:

(P) Host cells, comprising a readout system which allows host cells to be visually differentiated upon activation of said readout system; and

(Q) at least one genetic element comprising a selectable marker and genetic information encoding an activation domain or a DNA binding domain, which activation domain and DNA binding domain are together able to activate said readout system;

66. Kit according to claim 65, wherein said host cells are bacterial cells or mammalian cells.

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